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L8: Entry 2 of 13 File: USPT Dec 5, 2000

DOCUMENT-IDENTIFIER: US 6156733 A
TITLE: Use of leukemia inhibitory factor and endothelin antagonists

DATE FILED (1):
19980213

Abstract Text (1):
A leukemia inhibitory factor antagonist, alone or in combination with an endothelin antagonist, may be used for treatment of heart failure. The antagonist(s) are administered in a chronic fashion, in therapeutically effective amounts, to achieve this purpose.

Detailed Description Text (43):
Animals are immunized against the LIF or endothelin polypeptide or fragment, immunogenic conjugates, or derivatives by combining 1 mg or 1 .mu.g of the peptide or conjugate (for rabbits or mice, respectively) with 3 volumes of Freund's complete adjuvant and injecting the solution intradermally at multiple sites. One month later the animals are boosted with 1/5 to 1/10 the original amount of peptide or conjugate in Freund's complete adjuvant by subcutaneous injection at multiple sites. Seven to 14 days later the animals are bled and the serum is assayed for antibody titer to LIF or endothelin or a fragment thereof. Animals are boosted until the titer plateaus. Preferably, the animal is boosted with the conjugate of the same LIF or endothelin or fragment thereof, but conjugated to a different protein and/or through a different cross-linking reagent. Conjugates also can be made in recombinant cell culture as protein fusions. Also, aggregating agents such as alum are suitably used to enhance the immune response.

Detailed Description Text (104):
While polymers such as ethylene-vinyl acetate and lactic acid-glycolic acid enable release of molecules for over 100 days, certain hydrogels release proteins for shorter time periods. When encapsulated proteins remain in the body for a long time, they may denature or aggregate as a result of exposure to moisture at 37.degree. C., resulting in a loss of biological activity and possible changes in immunogenicity. Rational strategies can be devised for protein stabilization depending on the mechanism involved. For example, if the aggregation mechanism is discovered to be intermolecular S--S bond formation through thio-disulfide interchange, stabilization may be achieved by modifying sulfhydryl residues, lyophilizing from acidic solutions, controlling moisture content, using appropriate additives, and developing specific polymer matrix compositions.

Detailed Description Text (108):
The two types of antagonists, if used together, may be formulated together in an appropriate carrier vehicle to form a pharmaceutical composition that preferably does not contain cells. In one embodiment, the buffer used for formulation will depend on whether the composition will be employed immediately upon mixing or stored for later use, since long-term storage may bring into issue stability such as solubility and aggregation that can be addressed by altering the pH. The final preparation may be a stable liquid or lyophilized solid.

WEST Search History

DATE: Wednesday, December 04, 2002

Set Name side by side	Query	Hit Count	Set Name result set
DB=JPAB,EPAB,DWPI; PLUR=NO; OP=ADJ			
L12	L11 and (stability or stabilized or stabilizing or aggregat$3 or deamidat$3)	21	L12
L11	L10 or l9	441	L11
L10	D near factor	282	L10
L9	(leukemia or leukaemia) adj2 factor$1	159	L9
DB=USPT; PLUR=NO; OP=ADJ			
L8	L7 or l6	13	L8
L7	L5 and @prad<19981126	3	L7
L6	L5 and @ad<19981126	13	L6
L5	L4 and aggregat$3	14	L5
L4	L3[ti,ab]	72	L4
L3	L2 or l1	2009	L3
L2	D near factor	1247	L2
L1	(leukemia or leukaemia) adj2 factor$1	801	L1

END OF SEARCH HISTORY